WEST Search History

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DATE: Friday, May 19, 2006

Hide?	Set Name	Query	Hit Count
		DB=PGPB,USPT; PLUR=YES; OP=OR	
☐	L2	(((zvegf4 or pdgf adj d)) and (fibrosis or mesangia?))	51
☐	L1	((zvegf4 or pdgf adj d))	82

END OF SEARCH HISTORY

WEST Search History

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DATE: Friday, May 19, 2006

Hide?	Set Name	Query	Hit Count
		DB=EPAB,JPAB,DWPI; PLUR=YES; OP=OR	
☐	L4	L3 and (fibrosis or mesangia?)	2
☐	L3	zvegf4 or pdgf adj d	21
		DB=PGPB,USPT; PLUR=YES; OP=OR	
☐	L2	(((zvegf4 or pdgf adj d)) and (fibrosis or mesangia?))	51
☐	L1	((zvegf4 or pdgf adj d))	82

END OF SEARCH HISTORY

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 NEWS  1          Web Page URLs for STN Seminar Schedule - N. America
 NEWS  2          "Ask CAS" for self-help around the clock
 NEWS  3  JAN 17  Pre-1988 INPI data added to MARPAT
 NEWS  4  FEB 21  STN AnaVist, Version 1.1, lets you share your STN AnaVist
                  visualization results
 NEWS  5  FEB 22  The IPC thesaurus added to additional patent databases on STN
 NEWS  6  FEB 22  Updates in EPFULL; IPC 8 enhancements added
 NEWS  7  FEB 27  New STN AnaVist pricing effective March 1, 2006
 NEWS  8  MAR 03  Updates in PATDPA; addition of IPC 8 data without attributes
 NEWS  9  MAR 22  EMBASE is now updated on a daily basis
 NEWS 10  APR 03  New IPC 8 fields and IPC thesaurus added to PATDPAFULL
 NEWS 11  APR 03  Bibliographic data updates resume; new IPC 8 fields and IPC
                  thesaurus added in PCTFULL
 NEWS 12  APR 04  STN AnaVist $500 visualization usage credit offered
 NEWS 13  APR 12  LINSPEC, learning database for INSPEC, reloaded and enhanced
 NEWS 14  APR 12  Improved structure highlighting in FQHIT and QHIT display
                  in MARPAT
 NEWS 15  APR 12  Derwent World Patents Index to be reloaded and enhanced during
                  second quarter; strategies may be affected
 NEWS 16  MAY 10  CA/CAplus enhanced with 1900-1906 U.S. patent records
 NEWS 17  MAY 11  KOREAPAT updates resume

 NEWS EXPRESS  FEBRUARY 15 CURRENT VERSION FOR WINDOWS IS V8.01a,
               CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 19 DECEMBER 2005.
               V8.0 AND V8.01 USERS CAN OBTAIN THE UPGRADE TO V8.01a AT
               http://download.cas.org/express/v8.0-Discover/

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=> file medline embase biosis caplus
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION
FULL ESTIMATED COST 0.21 0.21

FILE 'MEDLINE' ENTERED AT 12:30:19 ON 19 MAY 2006

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=> s zvegf4 or pdgf(w)d
L1 170 ZVEGF4 OR PDGF(W) D

=> s l1 and (fibrosis or mesangia?)
L2 53 L1 AND (FIBROSIS OR MESANGIA?)

=> dup rem l2
PROCESSING COMPLETED FOR L2
L3 20 DUP REM L2 (33 DUPLICATES REMOVED)

=> dis hi
'HI' IS NOT A VALID FORMAT
In a multifile environment, a format can only be used if it is valid in at least one of the files. Refer to file specific help messages or the STNGUIDE file for information on formats available in individual files.
REENTER DISPLAY FORMAT FOR ALL FILES (FILEDEFAULT):his
'HIS' IS NOT A VALID FORMAT
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REENTER DISPLAY FORMAT FOR ALL FILES (FILEDEFAULT):dis his
'DIS' IS NOT A VALID FORMAT
'HIS' IS NOT A VALID FORMAT
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REENTER DISPLAY FORMAT FOR ALL FILES (FILEDEFAULT):dis ibib abs l3 11-20
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'L11' IS NOT A VALID FORMAT
'11-20' IS NOT A VALID FORMAT
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or the STNGUIDE file for information on formats available in
individual files.
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REENTER DISPLAY FORMAT FOR ALL FILES (FILEDEFAULT):
REENTER DISPLAY FORMAT FOR ALL FILES (FILEDEFAULT):
REENTER DISPLAY FORMAT FOR ALL FILES (FILEDEFAULT):
REENTER DISPLAY FORMAT FOR ALL FILES (FILEDEFAULT):
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For information on display fields or formats for a specific file of
the multifile session, enter END to exit the DISPLAY command. Then at
the arrow prompt (=>), enter HELP DFIELDS FILE= followed by the file
name, e.g., HELP DFIELDS FILE=CAPLUS, or HELP FORMATS FILE=
followed by the name, e.g., HELP FORMAT FILE=COMPENDEX.
IF YOU REQUIRE FURTHER HELP, PLEASE CONTACT YOUR LOCAL HELP DESK
REENTER DISPLAY FORMAT FOR ALL FILES (FILEDEFAULT):

REENTER DISPLAY FORMAT FOR ALL FILES (FILEDEFAULT):
REENTER DISPLAY FORMAT FOR ALL FILES (FILEDEFAULT):
REENTER DISPLAY FORMAT FOR ALL FILES (FILEDEFAULT):ibib abs

L3 ANSWER 1 OF 20 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2006170498 IN-PROCESS
DOCUMENT NUMBER: PubMed ID: 16510766
TITLE: Antagonism of **PDGF**-D by human antibody CR002 prevents renal scarring in experimental glomerulonephritis.
AUTHOR: Ostendorf Tammo; Rong Song; Boor Peter; Wiedemann Stefanie; Kunter Uta; Haubold Ulrike; van Roeyen Claudia R C; Eitner Frank; Kawachi Hiroshi; Starling Gary; Alvarez Enrique; Smithson Glennda; Floege Jurgen
CORPORATE SOURCE: Division of Nephrology, University Hospital Aachen, Pauwelsstrasse 30, D-52074 Aachen, Germany.. tostendorf@ukaachen.de
SOURCE: Journal of the American Society of Nephrology : JASN, (2006 Apr) Vol. 17, No. 4, pp. 1054-62. Electronic Publication: 2006-03-01.
Journal code: 9013836. ISSN: 1046-6673.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: NONMEDLINE; IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 28 Mar 2006
Last Updated on STN: 15 Apr 2006
AB Glomerular **mesangial** cell proliferation and/or matrix accumulation characterizes many progressive renal diseases. **PDGF**-D was identified recently as a novel mediator of **mesangial** cell proliferation in vitro and in vivo. This study investigated the long-term consequences of **PDGF**-D inhibition in vivo. Rats with progressive mesangioproliferative glomerulonephritis (uninephrectomy plus anti-Thy-1.1 antibody) received the **PDGF**-D-neutralizing, fully human mAb CR002 on days

3, 10, and 17 after disease induction. Glomerular mesangioproliferative changes on day 10 were significantly reduced by anti-**PDGF-D** treatment as compared with control antibody. Eight weeks after disease induction, anti-**PDGF-D** therapy significantly ameliorated focal segmental glomerulosclerosis, podocyte damage (de novo desmin expression), tubulointerstitial damage, and **fibrosis** as well as the accumulation of renal interstitial matrix including type III collagen and fibronectin. Treatment with anti-**PDGF-D** also reduced the cortical infiltration of monocytes/macrophages on day 56, possibly related to lower renal cortical complement activation (C5b-9 deposition) and/or reduced epithelial-to-mesenchymal transition (preserved cortical expression of E-cadherin and reduced expression of vimentin and alpha-smooth muscle actin). In conclusion, these data provide evidence for a causal role of **PDGF-D** in the pathogenesis of renal scarring and point to a new therapeutic approach to progressive mesangioproliferative renal disease.

=> dis his

(FILE 'HOME' ENTERED AT 12:30:06 ON 19 MAY 2006)

FILE 'MEDLINE, EMBASE, BIOSIS, CAPLUS' ENTERED AT 12:30:19 ON 19 MAY 2006
L1 170 S ZVEGF4 OR PDGF(W)D
L2 53 S L1 AND (FIBROSIS OR MESANGIA?)
L3 20 DUP REM L2 (33 DUPLICATES REMOVED)

=> dis ibib abs 11-20 l3

L3 ANSWER 11 OF 20 MEDLINE on STN DUPLICATE 9
ACCESSION NUMBER: 2003454180 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14514732
TITLE: Obstructive uropathy in mice and humans: potential role for **PDGF-D** in the progression of tubulointerstitial injury.
AUTHOR: Taneda Sekiko; Hudkins Kelly L; Topouzis Stavros; Gilbertson Debra G; Ophascharoensuk Vuddhidej; Truong Luan; Johnson Richard J; Alpers Charles E
CORPORATE SOURCE: Department of Pathology, University of Washington, Seattle, Washington, USA.
CONTRACT NUMBER: DK47959 (NIDDK)
SOURCE: Journal of the American Society of Nephrology : JASN, (2003 Oct) Vol. 14, No. 10, pp. 2544-55.
Journal code: 9013836. ISSN: 1046-6673.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200409
ENTRY DATE: Entered STN: 30 Sep 2003
Last Updated on STN: 15 Sep 2004
Entered Medline: 14 Sep 2004
AB Tubulointerstitial **fibrosis** is a major characteristic of progressive renal diseases. Platelet-derived growth factor (PDGF) is a family of growth regulatory molecules consisting of PDGF-A and -B, along with the newly discovered PDGF-C and -D. They signal through cell membrane receptors, PDGF receptor alpha (PDGF-Ralpha) and receptor beta (PDGF-Rbeta). Involvement of PDGF-B and PDGF-Rbeta in the initiation and progression of renal **fibrosis** has been well documented. The authors studied the localization of PDGF ligands and receptors by immunohistochemistry, with emphasis on the role of **PDGF-D** in murine renal **fibrosis** induced by unilateral ureteral obstruction (UUO). In mice with UUO, de novo expression of **PDGF-D** was detected in interstitial cells at day 4,

which increased to maximal expression at day 14. Increased expression of PDGF-B by interstitial cells and in some tubules was observed after day 4. The diseased mice did not show augmentation of PDGF-A or PDGF-C proteins in the areas of **fibrosis**. PDGF-Ralpha and -Rbeta protein expression was increased in interstitial cells after day 4 and reached maximal expression at day 14. Human renal nephrectomies (n = 10) of chronic obstructive nephropathy demonstrated similar de novo expression of **PDGF-D** in interstitial cells, correlating with expression of PDGF-Rbeta and PDGF-B, as it did in the murine model. These observations suggest that **PDGF-D** plays an important role in the pathogenesis of tubulointerstitial injury through binding of PDGF-Rbeta in both human obstructive nephropathy and the corresponding murine model of UUO.

L3 ANSWER 12 OF 20 MEDLINE on STN DUPLICATE 10
ACCESSION NUMBER: 2003398231 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12937299
TITLE: A fully human monoclonal antibody (CR002) identifies **PDGF-D** as a novel mediator of mesangioproliferative glomerulonephritis.
AUTHOR: Ostendorf Tammo; van Roeyen Claudia R C; Peterson Jeffrey D; Kunter Uta; Eitner Frank; Hamad Avin J; Chan Gerlinde; Jia Xiao-Chi; Macaluso Jennifer; Gazit-Bornstein Gadi; Keyt Bruce A; Lichenstein Henri S; LaRochelle William J; Floege Jurgen
CORPORATE SOURCE: Division Nephrology, University of Aachen, Germany.
SOURCE: Journal of the American Society of Nephrology : JASN, (2003 Sep) Vol. 14, No. 9, pp. 2237-47.
Journal code: 9013836. ISSN: 1046-6673.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200402
ENTRY DATE: Entered STN: 26 Aug 2003
Last Updated on STN: 5 Feb 2004
Entered Medline: 4 Feb 2004

AB PDGF-B is of central importance in mesangioproliferative diseases. **PDGF-D**, a new PDGF isoform, like PDGF-B, signals through the PDGF betabeta-receptor. The present study first determined that **PDGF-D** is mitogenic for rat **mesangial** cells and is not inhibited by a PDGF-B antagonist. Low levels of **PDGF-D** mRNA were detected in normal rat glomeruli. After induction of mesangioproliferative nephritis in rats by anti-Thy 1.1 mAb, glomerular **PDGF-D** mRNA and protein expression increased significantly from days 4 to 9 in comparison with nonnephritic rats. Peak expression of **PDGF-D** mRNA occurred 2 d later than peak PDGF-B mRNA expression. In addition, **PDGF-D** serum levels increased significantly in the nephritic animals on day 7. For investigating the functional role of **PDGF-D**, neutralizing fully human mAb were generated using the XenoMouse technology. Rats with anti-Thy 1.1-induced nephritis were treated on days 3 and 5 with different amounts of a fully human PDGF-DD-specific neutralizing mAb (CR002), equal amounts of irrelevant control mAb, or PBS by intraperitoneal injection. Specific antagonism of **PDGF-D** led to a dose-dependent (up to 67%) reduction of glomerular cell proliferation. As judged by double immunostaining for 5-bromo-2'-deoxyuridine and alpha-smooth muscle actin, glomerular **mesangial** cell proliferation was reduced by up to 57%. Reduction of glomerular cell proliferation in the rats that received CR002 was not associated with reduced glomerular expression of PDGF-B mRNA. **PDGF-D** antagonism also led to reduced glomerular infiltration of monocytes/macrophages (day 5) and reduced accumulation of fibronectin (day 8). In contrast, no effect was noted in normal rats that

received an injection of CR002. These data show that PDGF-D is overexpressed in mesangioproliferative states and can act as an auto-, para-, or even endocrine glomerular cell mitogen, indicating that antagonism of PDGF-D may represent a novel therapeutic approach to mesangioproliferative glomerulonephritides.

L3 ANSWER 13 OF 20 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 2004:120841 BIOSIS
DOCUMENT NUMBER: PREV200400118299
TITLE: Modulation of renal growth factor expression by Fcgamma receptor status in cryoglobulin-associated membranoproliferative glomerulonephritis.
AUTHOR(S): Muhlfeld, Anja S. [Reprint Author]; Segerer, Stephan; Hudkins, Kelly L. [Reprint Author]; Carling, Matthew D. [Reprint Author]; Farr, Andrew G.; Ravetch, Jeffrey V.; Alpers, Charles E. [Reprint Author]
CORPORATE SOURCE: Pathology, University of Washington, Seattle, WA, USA
SOURCE: Journal of the American Society of Nephrology, (November 2003) Vol. 14, No. Abstracts Issue, pp. 639A. print. Meeting Info.: Meeting of the American Society of Nephrology Renal Week. San Diego, CA, USA. November 12-17, 2003. American Society of Nephrology. CODEN: JASNEU. ISSN: 1046-6673.
DOCUMENT TYPE: Conference; (Meeting)
Conference; (Meeting Poster)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 3 Mar 2004
Last Updated on STN: 3 Mar 2004

L3 ANSWER 14 OF 20 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 2004:120712 BIOSIS
DOCUMENT NUMBER: PREV200400118203
TITLE: Obstructive uropathy in mice and humans: Potential role for PDGF-D in the progression of tubulointerstitial injury.
AUTHOR(S): Taneda, Sekiko [Reprint Author]; Hudkins, Kelly L. [Reprint Author]; Topouzis, Stavros; Gilbertscn, Debra G.; Ophascharoensuk, Vuddhidej; Truong, Luan; Johnson, Richard J.; Alpers, Charles E. [Reprint Author]
CORPORATE SOURCE: Department of Pathology, University of Washington, Seattle, WA, USA
SOURCE: Journal of the American Society of Nephrology, (November 2003) Vol. 14, No. Abstracts Issue, pp. 628A. print. Meeting Info.: Meeting of the American Society of Nephrology Renal Week. San Diego, CA, USA. November 12-17, 2003. American Society of Nephrology. CODEN: JASNEU. ISSN: 1046-6673.
DOCUMENT TYPE: Conference; (Meeting)
Conference; (Meeting Poster)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 3 Mar 2004
Last Updated on STN: 3 Mar 2004

L3 ANSWER 15 OF 20 MEDLINE on STN DUPLICATE 11

ACCESSION NUMBER: 2003357706 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12890490
TITLE: A novel murine PDGF-D splicing variant results in significant differences in peptide expression and function.
AUTHOR: Zhuo Ying; Hoyle Gary W; Zhang Jian; Morris Gilbert; Lasky

Joseph A
CORPORATE SOURCE: Tulane University Health Sciences Center, Departments of Medicine and Pathology, 1430 Tulane Avenue, New Orleans, LA 70112-2699, USA.
SOURCE: Biochemical and biophysical research communications, (2003 Aug 15) Vol. 308, No. 1, pp. 126-32.
Journal code: 0372516. ISSN: 0006-291X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200309
ENTRY DATE: Entered STN: 1 Aug 2003
Last Updated on STN: 4 Sep 2003
Entered Medline: 3 Sep 2003

AB Platelet-derived growth factor (PDGF) is a potent mesenchymal cell mitogen and chemoattractant involved in the pathogenesis of fibroproliferative diseases. There are four known PDGF ligand isoforms designated A-D, two of which, C and D, were only recently discovered. We have identified a splicing variant in the **PDGF**-D isoform that occurs in mice, but not in humans. The presence of the splicing variant in murine **PDGF-D** appears to be due to an aberration in the splicing site at the junction of exons 5 and 6. The splicing variant results in a deletion predicted to have significant effects on peptide activity since it results in the deletion of bases within the cysteine knot domain that are important for peptide dimerization and receptor binding. It is important to appreciate differences between murine and human PDGF gene expression because PDGF is a key mitogen in the pathogenesis of **fibrosis** and mice are commonly employed as models for human disease.

L3 ANSWER 16 OF 20 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:540192 CAPLUS
DOCUMENT NUMBER: 137:104171
TITLE: **PDGF** D polypeptides, nucleic acids encoding them, and therapeutic or diagnostic applications of the polypeptides or their antibodies
INVENTOR(S): Shimkets, Richard A.; Lichenstein, Henri; Herrmann, John L.; Boldog, Ferenc L.; Minskoff, Stacey; Jeffers, Michael; Andrews, David; La Rochelle, William
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 97 pp., Cont.-in-part of U.S. Ser. No. 715,332.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 165
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002094546	A1	20020718	US 2001-775482	20010202
WO 2002059618	A2	20020801	WO 2001-US48901	20011116
WO 2002059618	A3	20030508		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2005200106	A1	20050210	AU 2005-200106		20050112
PRIORITY APPLN. INFO.:			US 1999-158083P	P	19991007
			US 1999-159231P	P	19991013
			US 2000-174485P	P	20000104
			US 2000-186707P	P	20000303
			US 2000-188250P	P	20000310
			US 2000-223879P	P	20000808
			US 2000-234082P	P	20000920
			US 2000-688312	A2	20001013
			US 2000-715332	A2	20001116
			AU 2000-37360	A3	20000309

AB Disclosed are novel PDGFD nucleic acids encoding proteins and polypeptides related to bone morphogenetic protein-1 (BMF1), to vascular endothelial growth factor E (VEGF-E) and to platelet derived growth factor (PDGF). Also disclosed are vectors, host cells, antibodies, and recombinant methods for producing these nucleic acids and polypeptides. Methods of use include detecting and staging of cancers. The claims of this continuation-in-part patent specifically claim a method of detecting the presence of at least one PDGFD antigen in a sample, comprising the steps of: (a) providing a biol. sample; (b) contacting the sample with an agent that binds the antigen; and (c) detecting the presence of the agent bound to the antigen; whereby the presence of the agent indicates that the antigen is present in the sample. A method contributing to a diagnosis of cancer in a subject based on the presence of a PDGFD antigen in a sample from the subject is also claimed, as is a method of staging cancer in a subject. Addnl. claimed are a method of phosphorylating a tyrosine residue of a cellular receptor comprising the step of contacting a cell harboring the receptor with a PDGFD polypeptide, a method of stimulating a response in a cell that is specific for a PDGF beta receptor comprising contacting the cell with a PDGFD polypeptide, and a method of inhibiting the growth of a cell by contacting the cell with an agent that specifically binds a PDGFD polypeptide. An isolated nucleic acid comprising a sequence encoding a PDGFD polypeptide and a method of preparing the PDGFD polypeptide are also claimed.

L3 ANSWER 17 OF 20 MEDLINE on STN DUPLICATE 12

ACCESSION NUMBER:	2002667552 MEDLINE
DOCUMENT NUMBER:	PubMed ID: 12427128
TITLE:	Platelet-derived growth factor-D expression in developing and mature human kidneys.
AUTHOR:	Changsirikulchai Siribha; Hudkins Kelly L; Goodpaster Tracy A; Volpone John; Topouzis Stavros; Gilbertson Debra G; Alpers Charles E
CORPORATE SOURCE:	Department of Medicine, Srinakharinwirot University, Bangkok, Thailand.
CONTRACT NUMBER:	DK47959 (NIDDK)
SOURCE:	Kidney international, (2002 Dec) Vol. 62, No. 6, pp. 2043-54. Journal code: 0323470. ISSN: 0085-2538.
PUB. COUNTRY:	United States
DOCUMENT TYPE:	Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:	English
FILE SEGMENT:	Priority Journals
OTHER SOURCE:	GENBANK-AF336376
ENTRY MONTH:	200305
ENTRY DATE:	Entered STN: 13 Nov 2002 Last Updated on STN: 24 May 2003 Entered Medline: 23 May 2003

AB BACKGROUND: Platelet-derived growth factor (PDGF) is a family of growth regulatory molecules composed of sulfide-bonded dimeric structures. Two well-studied PDGF peptides (PDGF-A and PDGF-B) have been shown to mediate a wide range of biological effects. PDGF-D is a newly recognized member of the PDGF family. Initial studies of the PDGF -D gene found its expression in cells of the vascular wall,

suggesting that it could participate in vascular development and pathology. However, its localization in human kidney tissues has never been studied. METHODS: **PDGF-D** expression in fetal (N = 30) and adult (N = 25) human kidney tissues was examined by immunohistochemistry using an affinity-purified antibody raised to human **PDGF-D**. Antibody absorption with the immunizing peptide was employed to confirm the specificity of this antibody. **PDGF-D** protein and gene expression in human kidneys also were demonstrated by Western blotting and reverse transcription-polymerase chain reaction (RT-PCR). RESULTS: In the developing kidney, **PDGF-D** was first expressed by epithelial cells of comma- and S-shaped structures of the developing nephron, and most consistently in the visceral epithelial cells in the later stages of glomerular differentiation. In addition, **PDGF-D** could be found in mesenchymal, presumptively fibroblast cells in the interstitium of developing renal pelvis and in fetal smooth muscle cells in arterial vessels. In the adult normal kidney, **PDGF-D** was expressed by the visceral epithelial cells. There was persistent expression in arterial smooth muscle cells as well as in some neointimal smooth muscle cells of arteriosclerotic vessels, and expression in smooth muscle cells of vasa rectae in the medulla. **PDGF-D** could be identified at the basolateral membrane of some injured tubules in areas of chronic tubulointerstitial injury routinely encountered in aging kidneys. Western blotting of homogenates of adult kidneys demonstrated monospecific bands at 50 kD corresponding to previously established size parameter for this protein. RT-PCR of human kidney RNA resulted in a 918 basepair band, the sequence of which corresponded to human **PDGF-D** (Genbank number AF336376). CONCLUSIONS: To our knowledge, these are the first studies to localize **PDGF-D** in human kidneys and suggest that **PDGF-D** may have a role in kidney development. **PDGF-D** was shown to bind to PDGF beta receptor, which localizes to **mesangial** cells, parietal epithelial cells, and interstitial fibroblasts, suggesting potential paracrine interactions between those cells and the visceral epithelium.

L3 ANSWER 18 OF 20 MEDLINE on STN

ACCESSION NUMBER: 2003119490 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12632922
TITLE: [Structure and function of PDGF-R-alpha and its expression in normal kidney and kidney diseases].
Budowa i funkcja PDGF-alpha r oraz jego ekspresja w nerce prawidlowej i nerkach zmienionych chorobowo.
AUTHOR: Miller-Kasprzak Ewa; Niemir Zofia I; Czekalski Stanislaw
CORPORATE SOURCE: Pracownia Nefrologii Molekularnej Katedry i Kliniki Nefrologii Akademii Medyczne w Poznaniu.
SOURCE: Przegla d lekarski, (2002) Vol. 59, No. 10, pp. 826-31.
Ref: 46
Journal code: 19840720R. ISSN: 0033-2240.
PUB. COUNTRY: Poland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: Polish
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200305
ENTRY DATE: Entered STN: 14 Mar 2003
Last Updated on STN: 16 May 2003
Entered Medline: 15 May 2003

AB Platelet-derived growth factor is commonly known as a mitogen. Many research data suggest a role for PDGF-beta R in the mitogenic response of **mesangial** cells. There are four members of PDGF family known as PDGF-A chain, PDGF-B chain, PDGF-C chain and **PDGF-D** chain, which in active forms are dimers. As far as two receptors PDGF-alpha R and PDGF-beta R are known to bind PDGF. There is a difference in binding affinity of various forms of PDGF by these

receptors. Two different promotors P1 and P2 can be used for PDGF-alpha R gene transcription. There are several different haplotypes of promotor P1 sequence. Transcription of PDGF-alpha R gene is under control of many factors. Interaction between a receptor and its ligand includes receptor dimerisation and autophosphorylation of tyrosine residues. PDGF AA is unique in that it can only be bound by alpha-receptor dimer. PDGF-AA expression has been confirmed in the normal kidney, as well as in several renal diseases. Although the expression of PDGF-alpha R has been found to accompany that of PDGF-AA, its actual relevance for the development of the glomerular pathology is not clear.

L3 ANSWER 19 OF 20 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:102055 CAPLUS
DOCUMENT NUMBER: 136:289109
TITLE: New members of the platelet-derived growth factor family of mitogens
AUTHOR(S): Heldin, Carl-Henrik; Eriksson, Ulf; Oestman, Arne
CORPORATE SOURCE: Biomedical Center, Ludwig Institute for Cancer Research, Uppsala, SE-751 24, Swed.
SOURCE: Archives of Biochemistry and Biophysics (2002), 398(2), 284-290
CODEN: ABBIA4; ISSN: 0003-9861
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review is given on the structural and functional properties of the 2 novel members of the platelet-derived growth factor (PDGF) family, PDGF-C and **PDGF-D**. The PDGF-CC isoform has similar receptor binding-specificity as PDGF-AA and PDGF-DD binds only to PDGF β-receptors which differs from PDGF-BB, which binds both to α- and β-receptors. The different expression patterns of the two new PDGF isoforms during the embryonal development indicates that the different PDGF isoforms may have different functions. The PDGF-CC and PDGF-DD isoforms may be involved in the development of various disorders. This idea is supported by the finding that overexpression in the heart leads to heart hypertrophy and **fibrosis** with a phenotype similar to human heart **fibrosis**. (c) 2002 Academic Press.
REFERENCE COUNT: 69 THERE ARE 69 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 20 OF 20 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2002:567516 BIOSIS
DOCUMENT NUMBER: PREV200200567516
TITLE: **Mesangial** proliferative glomerulopathy induced by **PDGF-D** resulting from adenovirus mediated gene transfer.
AUTHOR(S): Hudkins, Kelly L. [Reprint author]; Gilbertson, Debra G.; Hughes, Steven E.; Holden, Matthew; Palmer, Thomas E.; Feldhaus, Andrew L.; Alpers, Charles E. [Reprint author]
CORPORATE SOURCE: Pathology, University of Washington, Seattle, WA, USA
SOURCE: Journal of the American Society of Nephrology, (September, 2002) Vol. 13, No. Program and Abstracts Issue, pp. 132A. print.
Meeting Info.: Meeting of the American Society of Nephrology. Philadelphia, PA, USA. October 30-November 04, 2002. American Society of Nephrology.
CODEN: JASNEU. ISSN: 1046-6673.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 7 Nov 2002
Last Updated on STN: 7 Nov 2002

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L3 ANSWER 1 OF 20 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2006170498 IN-PROCESS
DOCUMENT NUMBER: PubMed ID: 16510766
TITLE: Antagonism of **PDGF**-D by human antibody CR002 prevents renal scarring in experimental glomerulonephritis.
AUTHOR: Ostendorf Tammo; Rong Song; Boor Peter; Wiedemann Stefanie; Kunter Uta; Haubold Ulrike; van Roeyen Claudia R C; Eitner Frank; Kawachi Hiroshi; Starling Gary; Alvarez Enrique; Smithson Glennda; Floege Jurgen
CORPORATE SOURCE: Division of Nephrology, University Hospital Aachen, Pauwelsstrasse 30, D-52074 Aachen, Germany.. tostendorf@ukaachen.de
SOURCE: Journal of the American Society of Nephrology : JASN, (2006 Apr) Vol. 17, No. 4, pp. 1054-62. Electronic Publication: 2006-03-01.
Journal code: 9013836. ISSN: 1046-6673.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: NONMEDLINE; IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 28 Mar 2006
Last Updated on STN: 15 Apr 2006

AB Glomerular **mesangial** cell proliferation and/or matrix accumulation characterizes many progressive renal diseases. **PDGF**-D was identified recently as a novel mediator of **mesangial** cell proliferation in vitro and in vivo. This study investigated the long-term consequences of **PDGF**-D inhibition in vivo. Rats with progressive mesangioproliferative glomerulonephritis (uninephrectomy plus anti-Thy-1.1 antibody) received the **PDGF**-D-neutralizing, fully human mAb CR002 on days 3, 10, and 17 after disease induction. Glomerular mesangioproliferative changes on day 10 were significantly reduced by anti-**PDGF**-D treatment as compared with control antibody. Eight weeks after disease induction, anti-**PDGF**-D therapy significantly ameliorated focal segmental glomerulosclerosis, podocyte damage (de novo desmin expression), tubulointerstitial damage, and **fibrosis** as well as the accumulation of renal interstitial matrix including type III collagen and fibronectin. Treatment with anti-**PDGF**-D also reduced the cortical infiltration of monocytes/macrophages on day 56, possibly related to lower renal cortical complement activation (C5b-9 deposition) and/or reduced epithelial-to-mesenchymal transition (preserved cortical expression of E-cadherin and reduced expression of vimentin and alpha-smooth muscle actin). In conclusion, these data provide evidence for a causal role of **PDGF**-D in the pathogenesis of renal scarring and point to a new therapeutic approach to progressive mesangioproliferative renal disease.

L3 ANSWER 2 OF 20 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2005601008 MEDLINE
DOCUMENT NUMBER: PubMed ID: 16279938
TITLE: Structural and functional specificities of PDGF-C and **PDGF**-D, the novel members of the platelet-derived growth factors family.
AUTHOR: Reigstad Laila J; Varhaug Jan E; Lillehaug Johan R
CORPORATE SOURCE: Department of Molecular Biology, University of Bergen, Norway.
SOURCE: The FEBS journal, (2005 Nov) Vol. 272, No. 22, pp. 5723-41. Ref: 112
Journal code: 101229646. ISSN: 1742-464X.
PUB. COUNTRY: England: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200512
ENTRY DATE: Entered STN: 11 Nov 2005
Last Updated on STN: 31 Dec 2005
Entered Medline: 30 Dec 2005

AB The platelet-derived growth factor (PDGF) family was for more than 25 years assumed to consist of only PDGF-A and -B. The discovery of the novel family members PDGF-C and **PDGF**-D triggered a search for novel activities and complementary fine tuning between the members of this family of growth factors. Since the expansion of the PDGF family, more than 60 publications on the novel PDGF-C and **PDGF**-D have been presented, highlighting similarities and differences to the classical PDGFs. In this paper we review the published data on the PDGF family covering structural (gene and protein) similarities and differences among all four family members, with special focus on PDGF-C and **PDGF**-D expression and functions. Little information on the protein structures of PDGF-C and -D is currently available, but the PDGF-C protein may be structurally more similar to VEGF-A than to PDGF-B. PDGF-C contributes to normal development of the heart, ear, central nervous system (CNS), and kidney, while **PDGF**-D is active in the development of the kidney, eye and brain. In adults, PDGF-C is active in the kidney and the central nervous system. **PDGF**-D also plays a role in the lung and in periodontal mineralization. PDGF-C is expressed in Ewing family sarcoma and **PDGF**-D is linked to lung, prostate and ovarian cancers. Both PDGF-C and -D play a role in progressive renal disease, glioblastoma/medulloblastoma and **fibrosis** in several organs.

L3 ANSWER 3 OF 20 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 2005604162 MEDLINE
DOCUMENT NUMBER: PubMed ID: 16224065
TITLE: Platelet-derived growth factor D induces cardiac **fibrosis** and proliferation of vascular smooth muscle cells in heart-specific transgenic mice.
AUTHOR: Ponten Annica; Folestad Erika Bergsten; Pietras Kristian; Eriksson Ulf
CORPORATE SOURCE: Ludwig Institute for Cancer Research, S-17177 Stockholm, Sweden.
SOURCE: Circulation research, (2005 Nov 11) Vol. 97, No. 10, pp. 1036-45. Electronic Publication: 2005-10-13. Journal code: 0047103. E-ISSN: 1524-4571.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200512
ENTRY DATE: Entered STN: 15 Nov 2005
Last Updated on STN: 18 Dec 2005
Entered Medline: 9 Dec 2005

AB Platelet-derived growth factor (**PDGF**)-D is a member of the PDGF/vascular endothelial growth factor family that activates PDGF receptor beta (PDGFR-beta). We show that **PDGF**-D is highly expressed in the myocardium throughout development and adulthood, as well as by arterial vascular smooth muscle cells (vSMCs). To obtain further knowledge regarding the in vivo response to **PDGF**-D, we generated transgenic mice overexpressing the active core domain of **PDGF**-D in the heart. Transgenic **PDGF**-D stimulates proliferation of cardiac interstitial fibroblasts and arterial vSMCs. This results in cardiac **fibrosis** followed by dilated cardiomyopathy and subsequent cardiac failure. Transgenic mice also display vascular remodeling, including dilation of

vessels, increased density of SMC-coated vessels, and proliferation of vSMCs, leading to a thickening of tunica media. The thickening of arterial walls is a unique feature of **PDGF-D**, because this is not seen when PDGF-C is overexpressed in the heart. These results show that **PDGF-D**, via PDGFR-beta signaling, is a potent modulator of both vascular and connective tissue growth and may provide both paracrine and autocrine stimulation of PDGFR-beta. Our data raise the possibility that this growth factor may be involved in cardiac **fibrosis** and atherosclerosis.

L3 ANSWER 4 OF 20 MEDLINE on STN
ACCESSION NUMBER: 2005667544 IN-PROCESS
DOCUMENT NUMBER: PubMed ID: 16354289
TITLE: Platelet derived growth factor-D may be a possible therapeutic target for advanced IgA nephropathy.
AUTHOR: Endoh Masayuki; Wu Qiong; Rifai Abdalla; Suzuki Daisuke; Yagame Mitsunori; Sakai Hideto
CORPORATE SOURCE: Division of Nephrology and Metabolism, Department of Internal Medicine, Tokai University School of Medicine, Isehara, Kanagawa, Japan.
SOURCE: Nephrology (Carlton, Vic.), (2005 Dec) Vol. 10 Suppl 6, pp. A439.
Journal code: 9615568. ISSN: 1320-5358.
PUB. COUNTRY: Australia
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: NONMEDLINE; IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 20 Dec 2005
Last Updated on STN: 27 Jan 2006

AB Severe **mesangial** proliferation was induced by over-expression of platelet derived growth factor-D (**PDGF-D**) in rodents. It was also demonstrated that administration of neutralizing antibody to **PDGF-D** attenuated glomerular damage and tubulo-interstitial damage in anti-Thy 1 with heminephrectomy model.We investigated mRNA expression of PDGF family and its receptor in IgA nephropathy (IgAN) and rapidly progressive glomerulonephritis (RPGN). Quantitative analysis was performed to measure the amount of mRNA of PDGF-A, B, C, D, alpha receptor and beta receptor using real-time PCR. Amount of actin mRNA was measured as internal control in each sample.The mRNA amount of PDGF-A, B (Fig. 1), C, alpha receptor and beta receptor except **PDGF-D** was almost ubiquitous from slight tissue damage and severe tissue damage in IgAN as well as RPGN. High **PDGF-D** mRNA expression was observed only in the tissues with severe histological damage of IgAN (**PDGF-D**/Actin ratio 2.5, Fig. 2). Very low **PDGF-D** mRNA was expressed in the tissues with slight histological damage of IgAN (**PDGF-D**/Actin ratio 0.4) and RPGN (**PDGF-D**/Actin ratio 0.7). Human proximal tubular cell line showed significant increase of **PDGF-D** mRNA expression after lipopolysaccharide (LPS) stimulation, although PDGF-C mRNA was expressed ubiquitously from unstimulated condition with slight increase after LPS stimulation.Immunohistological study demonstrated **PDGF-D** protein was abundant at interstitial fibrotic area in advanced tissues of IgAN (Fig. 3). **PDGF-D** was not shown at the **mesangial** proliferative area in IgAN.These findings suggest that **PDGF-D** might be a good molecular target for the treatment of advanced stage of human IgAN.

L3 ANSWER 5 OF 20 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 2005445381 MEDLINE
DOCUMENT NUMBER: PubMed ID: 16039137
TITLE: Expression patterns of PDGF-A, -B, -C and -D and the PDGF-receptors alpha and beta in activated rat hepatic stellate cells (HSC).

AUTHOR: Breitkopf Katja; Roeyen Claudia van; Sawitza Iris; Wickert Lucia; Floege Jurgen; Gressner Axel M
CORPORATE SOURCE: Department of Medicine II, Mol. Alcohol Research in Gastroenterology, University Hospital Mannheim, University of Heidelberg, Theodor-Kutzer-Ufer 1-3, 68167 Mannheim, Germany.. katja.breitkopf@med.ma.uni-heidelberg.de
SOURCE: Cytokine, (2005 Sep 7) Vol. 31, No. 5, pp. 349-57.
Journal code: 9005353. ISSN: 1043-4666.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200510
ENTRY DATE: Entered STN: 23 Aug 2005
Last Updated on STN: 19 Oct 2005
Entered Medline: 18 Oct 2005

AB The platelet-derived growth factor (PDGF) family, which regulates many physiological and pathophysiological processes has recently been enlarged by two new members, the isoforms PDGF-C and -D. Little is known about the expression levels of these new members in hepatic **fibrosis**. We therefore investigated by quantitative real time PCR (Taqman) the mRNA expression profiles of all four PDGF isoforms in transdifferentiating primary cultured hepatic stellate cells (HSC), an in vitro model system of hepatic fibrogenesis, either with or without stimulation of the cells with PDGF-BB or TGF-beta1. All four isoforms were expressed in HSC transdifferentiating to myofibroblast-like cells (MFB) albeit with different profiles: while PDGF-A mRNA exhibited minor fluctuations only, PDGF-B was rapidly down-regulated. In contrast, both PDGF-C and -D mRNA were strongly induced: PDGF-C up to 5 fold from day 2 to day 8 and **PDGF-D** up to 8 fold from day 2 to day 5 of culture.
Presence of PDGF-DD in activated HSC was confirmed at the protein level by immunocytochemistry. Stimulation of HSC and MFB with PDGF-BB led to down-regulation of the new isoforms, whereas TGF-beta1 upregulated PDGF-A only. We further show that PDGF receptor-beta (PDGFR-beta) mRNA was rapidly upregulated within the first day of culture and was constantly expressed from day 2 on while the expression profile of PDGFR-alpha mRNA was very similar to that of PDGF-A during transdifferentiation. Given the dramatic changes in PDGF-C and -D expression, which may compensate for down-regulation of PDGF-B, we hypothesize that the new PDGF isoforms may fulfil specific functions in hepatic fibrogenesis.

L3 ANSWER 6 OF 20 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 2004167258 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15061151
TITLE: PDGF C is a selective alpha platelet-derived growth factor receptor agonist that is highly expressed in platelet alpha granules and vascular smooth muscle.
AUTHOR: Fang Li; Yan Yibing; Komuves Laszlo G; Yonkovich Shirlee; Sullivan Carol M; Stringer Bradley; Galbraith Sarah; Lokker Nathalie A; Hwang S Stuart; Nurden Paquita; Phillips David R; Giese Neill A
CORPORATE SOURCE: Millennium Pharmaceuticals, South San Francisco, Calif 94080, USA.
SOURCE: Arteriosclerosis, thrombosis, and vascular biology, (2004 Apr) Vol. 24, No. 4, pp. 787-92.
Journal code: 9505803. E-ISSN: 1524-4636.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200408
ENTRY DATE: Entered STN: 6 Apr 2004
Last Updated on STN: 6 Aug 2004
Entered Medline: 5 Aug 2004

AB OBJECTIVE: The platelet-derived growth factor (PDGF) family consists of four members, PDGF A, PDGF B, and 2 new members, PDGF C and PDGF D, which signal through the alpha and beta PDGF receptor (PDGFR) tyrosine kinases. This study was performed to determine the receptor specificity and cellular expression profile of PDGF C. METHODS AND RESULTS: PDGF C growth factor domain (GFD) was shown to preferentially bind and activate alpha PDGFR and activate beta PDGFR when it is co-expressed with alpha PDGFR through heterodimer formation. An investigation of PDGF C mRNA and protein expression revealed that during mouse fetal development, PDGF C was expressed in the mesonephric mesenchyme, prefusion skeletal muscle, cardiac myoblasts, and in visceral and vascular smooth muscle, whereas in adult human tissues expression was largely restricted to smooth muscle. Microarray analysis of various cell types showed PDGF C expression in vascular smooth muscle cells, renal **mesangial** cells, and platelets. PDGF C mRNA expression in platelets was confirmed by real-time polymerase chain reaction, and PDGF C protein was localized in alpha granules by immuno-gold electron microscopy. Western blot analysis of platelets identified 55-kDa and 80-kDa PDGF C isoforms that were secreted on platelet activation. CONCLUSIONS: Taken together, our results demonstrated for the first time to our knowledge that like PDGF A and B, PDGF C is likely to play a role in platelet biology.

L3 ANSWER 7 OF 20 MEDLINE on STN DUPLICATE 6
ACCESSION NUMBER: 2004046351 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14747375
TITLE: Exogenous **PDGF-D** is a potent **mesangial** cell mitogen and causes a severe **mesangial** proliferative glomerulopathy.
AUTHOR: Hudkins Kelly L; Gilbertson Debra G; Carling Matthew; Taneda Sekiko; Hughes Steven D; Holdren Matthew S; Palmer Thomas E; Topouzis Stavros; Haran Aaron C; Feldhaus Andrew L; Alpers Charles E
CORPORATE SOURCE: University of Washington, Seattle, Washington 98195, USA.
CONTRACT NUMBER: DK 47659 (NIDDK)
SOURCE: Journal of the American Society of Nephrology : JASN, (2004 Feb) Vol. 15, No. 2, pp. 286-98.
Journal code: 9013836. ISSN: 1046-6673.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200409
ENTRY DATE: Entered STN: 29 Jan 2004
Last Updated on STN: 21 Sep 2004
Entered Medline: 20 Sep 2004

AB The PDGF family consists of at least four members, PDGF-A, -B, -C, and -D. All of the PDGF isoforms bind and signal through two known receptors, PDGF receptor-alpha and PDGF receptor-beta, which are constitutively expressed in the kidney and are upregulated in specific diseases. It is well established that PDGF-B plays a pivotal role in the mediation of glomerular **mesangial** cell proliferation. However, little is known of the roles of the recently discovered PDGF-C and -D in mediating renal injury. In this study, adenovirus constructs encoding PDGF-B, -C, and -D were injected into mice. Mice with high circulating levels of **PDGF-D** developed a severe **mesangial** proliferative glomerulopathy, characterized by enlarged glomeruli and a striking increase in glomerular cellularity. The PDGF-B-overexpressing mice had a milder proliferative glomerulopathy, whereas the mice overexpressing PDGF-C and those that received adenovirus alone showed no measurable response. Mitogenicity of **PDGF-D** and -B for **mesangial** cells was confirmed in vitro. These findings emphasize the importance of engagement of PDGF receptor-beta in transducing **mesangial** cell proliferation and demonstrate that

PDGF-D is a major mediator of mesangial cell proliferation. Finally, this approach has resulted in a unique and potentially valuable model of mesangial proliferative glomerulopathy and its resolution.

L3 ANSWER 8 OF 20 MEDLINE on STN DUPLICATE 7
ACCESSION NUMBER: 2003576232 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12972405
TITLE: Modulation of PDGF-C and PDGF-D expression during bleomycin-induced lung fibrosis .
AUTHOR: Zhuo Ying; Zhang Jian; Laboy Miguel; Lasky Joseph A
CORPORATE SOURCE: Department of Medicine, Tulane University Health Sciences Center, 1430 Tulane Ave., New Orleans, LA 70112, USA.
SOURCE: American journal of physiology. Lung cellular and molecular physiology, (2004 Jan) Vol. 286, No. 1, pp. L182-8. Electronic Publication: 2003-09-12. Journal code: 100901229. ISSN: 1040-0605.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200402
ENTRY DATE: Entered STN: 16 Dec 2003
Last Updated on STN: 7 Feb 2004
Entered Medline: 6 Feb 2004
AB PDGF isoforms are a family of polypeptides that bind to cell surface receptors and induce fibroblast proliferation and chemotaxis. The PDGF-A and -B chain isoforms have been implicated in fibroproliferative lung injury in animal models and in human disease. Two recently recognized PDGF polypeptides, PDGF-C and -D, differ from the PDGF-A and -B isoforms in that they require proteolytic cleavage before they can bind and activate the PDGF receptors. Our findings demonstrate that administration of bleomycin to murine lungs leads to a significant increase in PDGF-C mRNA expression and a significant decrease in PDGF-D mRNA expression. PDGF-C expression was localized to areas of lung injury by in situ hybridization, and PDGF-C expression was not upregulated in the lungs of BALB/c mice that are resistant to bleomycin-induced lung fibrosis. Moreover, there is in vivo phosphorylation of the PDGF-receptor that binds PDGF-C in response to bleomycin administration. These observations strongly suggest a role for PDGF-C in bleomycin-induced pulmonary fibrosis.

L3 ANSWER 9 OF 20 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN DUPLICATE 8
ACCESSION NUMBER: 2004127812 EMBASE
TITLE: PDGF-D: A novel mediator of mesangioproliferative glomerulonephritis.
AUTHOR: Floege J.; Van Roeyen C.; Ostendorf T.
CORPORATE SOURCE: Dr. J. Floege, Medizinische Klinik II, Klinikum der RWTH, Pauwelsstr. 30, D-52074 Aachen, Germany. Juergen.Floege@rwth-aachen.de
SOURCE: Drugs of the Future, (2004) Vol. 29, No. 2, pp. 179-184. . Refs: 47
ISSN: 0377-8282 CODEN: DRFUD4
COUNTRY: Spain
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
006 Internal Medicine
028 Urology and Nephrology
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 12 Apr 2004

Last Updated on STN: 12 Apr 2004

AB In view of the increasing number of patients with end-stage renal disease (ESRD), new approaches to common underlying diseases such as mesangioproliferative glomerulonephritis, including IgA nephropathy, are urgently needed. Whereas the role of platelet-derived growth factor (PDGF) B-chain (PDGF-B) in mediating mesangioproliferative changes is well established, the role of **PDGF** D-chain (**PDGF**-D) has only recently been elucidated. Like PDGF-B, **PDGF**-D signals through the PDGF β-receptor and therefore shares a number of biological activities with PDGF-B. Recent studies have shown that **PDGF-D** induces **mesangial** cell proliferation in vitro and is overexpressed in mesangioproliferative glomerulonephritis in vivo. In addition, hepatic transfection with a **PDGF-D** expression plasmid induced prominent mesangiopro-liferative nephritis in mice, whereas antagonism of **PDGF-D** in a rat model of mesangioproliferative disease ameliorated the renal changes. These observations establish **PDGF**-D, along with PDGF-B, as an important mediator of mesangioproliferative nephritis in vivo and suggest that it may be an attractive therapeutic target. In addition, preliminary observations suggest that **PDGF-D** may also contribute to secondary renal changes that characterize progressive renal failure, i.e., tubulointerstitial **fibrosis**.

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ACCESSION NUMBER: 2004020256 EMBASE
TITLE: Modulation of PDGF-C and **PDGF-D** expression during bleomycin-induced lung **fibrosis**.
AUTHOR: Zhuo Y.; Zhang J.; Laboy M.; Lasky J.A.
CORPORATE SOURCE: J.A. Lasky, Tulane Univ. Health Sciences Center, Dept. of Medicine, 1430 Tulane Ave., New Orleans, LA 70112, United States. jlasky@tulane.edu
SOURCE: American Journal of Physiology - Lung Cellular and Molecular Physiology, (2004) Vol. 286, No. 1 30-1, pp. L182-L188. .
Refs: 17
ISSN: 1040-0605 CODEN: APLPE7
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20 Feb 2004
Last Updated on STN: 20 Feb 2004

AB PDGF isoforms are a family of polypeptides that bind to cell surface receptors and induce fibroblast proliferation and chemotaxis. The PDGF-A and -B chain isoforms have been implicated in fibroproliferative lung injury in animal models and in human disease. Two recently recognized PDGF polypeptides, PDGF-C and -D, differ from the PDGF-A and -B isoforms in that they require proteolytic cleavage before they can bind and activate the PDGF receptors. Our findings demonstrate that administration of bleomycin to murine lungs leads to a significant increase in PDGF-C mRNA expression and a significant decrease in **PDGF-D** mRNA expression. PDGF-C expression was localized to areas of lung injury by in situ hybridization, and PDGF-C expression was not upregulated in the lungs of BALB/c mice that are resistant to bleomycin-induced lung **fibrosis**. Moreover, there is in vivo phosphorylation of the PDGF-receptor that binds PDGF-C in response to bleomycin administration. These observations strongly suggest a role for PDGF-C in bleomycin-induced pulmonary **fibrosis**.